



Synthetic Communications

An International Journal for Rapid Communication of Synthetic Organic Chemistry

ISSN: 0039-7911 (Print) 1532-2432 (Online) Journal homepage: http://www.tandfonline.com/loi/lsyc20

AN EFFICIENT BIOMIMETIC CLEAVAGE OF GEM-DIACETATES TO ALDEHYDES BY β-CYCLODEXTRIN UNDER NEUTRAL CONDITIONS IN AQUEOUS MEDIUM*

M. Arjun Reddy , L. Rajender Reddy , N. Bhanumathi & K. Rama Rao

To cite this article: M. Arjun Reddy , L. Rajender Reddy , N. Bhanumathi & K. Rama Rao (2002) AN EFFICIENT BIOMIMETIC CLEAVAGE OF GEM-DIACETATES TO ALDEHYDES BY β -CYCLODEXTRIN UNDER NEUTRAL CONDITIONS IN AQUEOUS MEDIUM*, Synthetic Communications, 32:2, 273-277, DOI: <u>10.1081/SCC-120002012</u>

To link to this article: http://dx.doi.org/10.1081/SCC-120002012



Published online: 16 Aug 2006.

Submit your article to this journal \square

Article views: 32



View related articles 🗹

LT Citing articles: 9 View citing articles		w citing articles 🖸
--	--	---------------------

Full Terms & Conditions of access and use can be found at http://www.tandfonline.com/action/journalInformation?journalCode=lsyc20

SYNTHETIC COMMUNICATIONS, 32(2), 273–277 (2002)

AN EFFICIENT BIOMIMETIC CLEAVAGE OF *GEM*-DIACETATES TO ALDEHYDES BY β-CYCLODEXTRIN UNDER NEUTRAL CONDITIONS IN AQUEOUS MEDIUM*

M. Arjun Reddy, L. Rajender Reddy, N. Bhanumathi, and K. Rama Rao^\dagger

Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad, 500007, India

ABSTRACT

The cleavage of *gem*-diacetates to aldehydes, a widely used protecting group in organic synthesis, has been achieved for the first time under neutral conditions in aqueous medium using β -cyclodextrin as catalyst. The main advantage of the present methodology is that it can be used with compounds having a variety of functional groups since the cleavage is carriedout under neutral conditions in aqueous medium.

273

Copyright © 2002 by Marcel Dekker, Inc.

www.dekker.com

^{*}IICT Communication No. 4655.

[†]Corresponding author. E-mail: ramaraok@iict.ap.nic.in

ORDER		REPRINTS
-------	--	----------

ARJUN REDDY ET AL.

Selective protection and deprotection of carbonyl groups are of great significance in organic synthesis especially in multistep synthesis of natural products.1 Amongst various protecting groups, gem-diacetates have been recognized as the method of choice due to their easy installation and removal and their stability in a variety of reaction conditions. Apart from this, these gem-diacetates are useful synthetic intermediates in various organic transformations.^{2,3} However, most of the general methods used for the cleavage of these diacetates include various acidic reagents such as K10 clay,⁴ hydrochloric acid,⁵ sulfuric acid,⁶ BI₃-*N*,*N*-dimethyl aniline complex⁷ etc. as well as basic reagents such as sodium and potassium hydroxide.⁸ However, these are some severe limitations with the literature methods such as use of strong acidic or basic conditions, lower yields, longer reaction times etc. Keeping in view the limitations of the existing procedures, we felt the need to develop an alternate and mild approach under neutral conditions using water as the solvent, which is an environmentally benign one. In our effort to develop biomimetic approaches for chemical reactions involving cyclodextrins in water,⁹ we report herein, for the first time, a practical and efficient method for the cleavage of gemdiacetates to aldehyde catalysed by β-cyclodextrin under neutral conditions in aqueous medium.

Cyclodextrins (CDs) which are cyclic oligosaccharides with hydrophobic cavities exert microenvironmental effect leading to selective reactions. They catalyse reactions involving supramolecular catalysis through noncovalent bonding as seen in enzymes. These biomimetic reactions can be effectively carried out in water under neutral conditions without generating any toxic waste products. Thus, mimicking of biochemical selectivity which involves supramolecular catalysis with the reactions being carried out in water will be superior to chemical selectivity. This has prompted us to attempt the cleavage of *gem*-diacetates using CDs, as this is one of the most useful synthetic transformations (scheme).

$$R \xrightarrow{OAc} \xrightarrow{\beta-CD/H_2O} R-CHO$$

R= aromatic, aliphatic and heterocyclic

Scheme.

The reactions were carried out by dissolving β -cyclodextrin in water followed by the addition of *gem*-diacetate. The yields of the products were

Copyright @ Marcel Dekker, Inc. All rights reserved





ORDER		REPRINTS
-------	--	----------

CLEAVAGE OF GEM-DIACETATES TO ALDEHYDES

Table 1. Selective Cleavage of gem-Diacetates to Aldehydes Catalysed by β -Cyclodextrin

Ent	ry Substrate	Product ^a	Reaction Time(h)	Yield (%) ^b
1	CH(OA c) ₂	СНО	6	95
2	A cO	СНО	6	88
3	AcO $CH(OAc)_2$		6	89
4	H-CO	H-CO	7	85
5	BnQ		8	80
6	OB n CH(OA c) ₂	СНО	7	89
7	H ₃ CO UCH ₃ H ₃ CO OCH ₃	H ₃ CO OCH 3	8	80
8	CH(OAc) ₂	СНО	8	80
9	CI CH(OAc) ₂ CI		8	72
10	O O I O I O CH(OAc)₂	CHO CHO	7	92
пв	OC-HN		8	70
12	H₂C CH(OAc)₂	Н3ССНО	6	89
13	CH(OA c);	2 CHO	6	80
14	CH(OAc) ₂	СНО	8	71
15	H ₃ CO	H ₃ CO	6	90
16	∕∕∕CH(OA c) ₂	~~~сно	8	60
17	CH(OAc)2	Сно	6	65

------a: All the products were characterised by ¹H NMR, IR and Mass Spectroscopy b: Isolated Yields after purification.



275

ORDER		REPRINTS
-------	--	----------

ARJUN REDDY ET AL.

impressive (up to 95%) and these reactions can be efficiently carried out with only catalytic amount of cyclodextrin (0.1 mole of CD per mole of the substrate). The cyclodextrin can also be recovered and reused. These reactions do no take place in the absence of CD. This methodology apart from having the advantage of neutral conditions and aqueous medium is also compatible in the presence of various other functional groups such as *O*Me, *O*-Bn, *O*-Allyl, methylene dioxy, *O*Ac and *N*-Boc. However, the yields with aliphatic and heterocyclic *gem*-diacetates, are comparatively lower. Here, the role of CD appears to be to activate the acetyl group by hydrogen bonding, thus facilitating its cleavage in the presence of water. Though, this reaction takes place in the presence of α -CD also, β -CD will be the most preferred catalyst due to its easy accessibility and economic viability.

In conclusion, this biomimetic methodology is the first of its kind to be applied for the cleavage of *gem*-diacetates, one of the most commonly used protecting groups in organic synthesis, under neutral conditions in aqueous medium in the presence of β -cyclodextrin. This method is also compatible in the presence of other functional groups.

EXPERIMENTAL

¹H NMR spectra were recorded on Gemini-200 MHz spectrometer and mass spectra were observed on VG Autospect M. The IR spectra were recorded on NICOLET FT-IR. Spectrometer.

General Procedure for the Cleavage of gem-Diacetates in Aqueous Medium Using β -Cyclodextrin: In a typical procedure, to β -cyclodextrin (0.1 mmol) dissolved in 20 ml of water by heating at 60°C, was added gem-diacetate (1 mmol) in methanol (1 ml) and stirred at this temperature for the required length of time (table). The reaction mixture was cooled to room temperature and extracted with ethylacetate (3 × 20 ml). The combined organic extract was washed with water (2 × 10 ml), dried over anhydrous sodium sulphate and evaporated under reduced pressure to give the product. This was further purified by column chromatography on silica gel (100–200) using hexane: ethylacetate (90:10). The yields were in the range of (60–95%).

ACKNOWLEDGMENT

MAR and LRR thank CSIR, New Delhi, India, for the award of research fellowships.

Copyright © Marcel Dekker, Inc. All rights reserved

ORDER		REPRINTS
-------	--	----------

CLEAVAGE OF GEM-DIACETATES TO ALDEHYDES

REFERENCES

- 1. a) Kocienski, P.J.; *Protecting Groups*, Georg. Theieme Verrlag Stuttgart: New York, **1994**. b) Green, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, Wiley: New York, 2nd ed., **1991**.
- a) Sridher, B.B.; Amin, S.G. Synth. Commun. 1978, *8*, 117. b) Bankas, R.E.; Miller, J.A.; Nunn, M.J.; Stanley, P.; Weakley, T.J.R. Ullah, Z. J. Chem. Soc. Perkin Trans 1 1981, 1096.
- 3. a) Sandberg, M.; Sydnes, L.K. Tetrahedron Lett. **1998**, *39*, 6361. b) Heerden, F.R.; Huyser, J.J.; Willams B.D.G.; Holzapfel, C.W. Tetrahedron Lett. **1998**, *39*, 5281.
- 4. Li, T.-S.; Zhang, Z.-H.; Fu, C.-G. Tetrahedron Lett. 1997, 38, 3285.
- 5. Tsaug, S.M.; Wood, E.H.; Johnson, J.R. Org. Syn. 1955, coll. vol. 3, 141.
- 6. Lieberman, S.V.; Cannon, R. Org. Syn. 1951, Coll. vol 3. 441.
- 7. Narayana, C.; Padmanabhan, S.; Kabalka, G.W. Tetrahedron Lett. **1990**, *31*, 6977.
- Kochhar, K.S.; Bal. B.S.; Deshpande, R.P.; Rajadhyaksha, S.N.; Pinnick, H.W. J. Org. Chem. 1983, 48, 1765.
- a) Rama Rao, K.; Sattur, P.B. J. Chem. Soc. Chem. Commun. 1989, 342. b) Rama Rao, K.; Sampath Kumar, H.M. Synth. Commun. 1993, 23, 1877. c) Rama Rao, K.; Bhanumathi, N.; Rajender Reddy, L. Synth. Commun. 1999, 29, 1703. d) Rajender Reddy, L.; Arjun Reddy, M.; Bhanumathi, N.; Rama Rao, K. Synlett 2000, 339.

Received in the UK November 16, 2000



277

Request Permission or Order Reprints Instantly!

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the <u>U.S. Copyright Office</u> for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on <u>Fair Use in the Classroom</u>.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our <u>Website</u> User Agreement for more details.

Order now!

Reprints of this article can also be ordered at http://www.dekker.com/servlet/product/DOI/101081SCC120002012